CLAIMS

What is claimed is:

1. A method of modulating an Edg-1 receptor mediated biological activity, comprising contacting a cell expressing the Edg-1 receptor with an amount of a modulator of the Edg-1 receptor sufficient to modulate the Edg-1 receptor mediated biological activity, wherein the modulator is not a phospholipid.

2. A method of modulating an Edg-1 receptor mediated biological activity in a subject, comprising administering to the subject a therapeutically effective amount of a modulator of the Edg-1 receptor, wherein the modulator is not a phospholipid.

3. The method of Claim 1 or 2, wherein the modulator is an agonist.

4. The method of Claim 1 or 2, wherein the modulator is an antagonist.

5. The method of Claim 1 or 2, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-1 relative to other Edg receptors.

6. The method of Claim 1 or 2, wherein the modulator exhibits at least about 100 fold inhibitory selectivity for Edg-1 relative to other Edg receptors.

7. The method of Claim 1 or 2, wherein the modulator exhibits at least about 20 fold inhibitory selectivity for Edg-1 relative to other Edg receptors.

8. The method of Claim 1 or 2, wherein the inhibitor exhibits at least about 5 fold inhibitory selectivity for Edg-1 relative to other Edg receptors.

9. The method of Claim 1 or 2, wherein the inhibitor exhibits at least about 200 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5, Edg-6 and Edg-8 receptors.

10. The method of Claim 1 or 2, wherein the inhibitor exhibits at least about 100 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5, Edg-6 and Edg-8 receptors.

11. The method of Claim 1 or 2, wherein the inhibitor exhibits at least about 20 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5, Edg-6 and Edg-8 receptors.

12. The method of Claim 1 or 2, wherein the inhibitor exhibits at least about 5 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5, Edg-6 and Edg-8 receptors.

13. The method of Claim 1 or 2, wherein the biological activity is cell proliferation.

14. The method of Claim 13, wherein the inhibitor exhibits at least about 200 fold inhibitory selectivity for Edg-1 relative to other Edg receptors.

15. The method of Claim 13, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-1 relative to other Edg receptors.

16. The method of Claim 13, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5, Edg-6 and Edg-8 receptors.

17. The method of Claim 13, wherein the modulator exhibits at least about 20 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5, Edg-6 and Edg-8 receptors.

18. The method of Claim 13, wherein cell proliferation leads to ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colon cancer or prostrate cancer.

19. The method of Claim 13, wherein cell proliferation is stimulated by S1P.

20. The method of Claim 1 or 2, wherein the biological activity is calcium mobilization, VEGF synthesis, IL-8 synthesis, platelet activation, cell migration, phosphoinositide hydrolysis, inhibition of cAMP formation, increasing the level of fatty acids, actin polymerization, apoptosis, angiogenesis, inhibition of wound healing, inflammation, expression of

endogenous protein growth factors, cancer invasiveness, vasoconstriction or atherogenesis.

21. The method of Claim 1 or 2 wherein the modulator binds to the Edg-1 receptor with a binding constant between about 10 μM to about 1 fM.

22. The method of Claim 1 or 2 wherein the modulator binds to the Edg-1 receptor with a binding constant of at least about 1 μM.

23. The method of Claim 1 or 2 wherein the modulator binds to the Edg-1 receptor with a binding constant of at least about 10 nM.

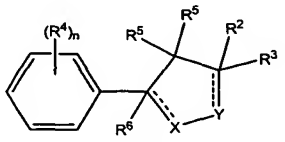
24. The method of Claim 1 or 2, wherein the modulator is a nucleic acid, peptide or carbohydrate.

25. The method of Claim 1 or 2, wherein the modulator is an organic molecule of molecular weight of less than 750 daltons.

26. The method of Claim 1, wherein the cell is a HTC hepatoma cell, an ovarian cell, an epithelial cell, a fibroblast cell, a neuronal cell, a carcinoma cell, a pheochromocytoma cell, a myoblast cell, a platelet cell or a fibrosarcoma cell.

27. The method of Claim 21, wherein the cell is OV202 human ovarian cell, a HTC rat hepatoma cell, a CAOV-3 human ovarian cancer cell, MDA-MB-453 breast cancer cell, MDA-MB-231 breast cancer cell, HUVEC cells A431 human epitheloid carcinoma cell or a HT-1080 human fibrosarcoma cell.

28. The method of Claim 1 or 2, wherein the modulator is a compound of structural formula (I):



(I)

or a pharmaceutically available solvate or hydrate thereof, wherein:

n = 0, 1, 2, 3, 4 or 5;

X is CR^5 or N;

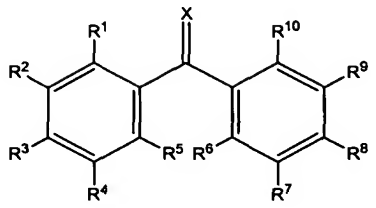
Y is CR^5R^5 or NR^1;

R^1 is either absent or hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, or substituted heteroalkyl;

R^2, R^3 and each R^5 are independently hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro or thio; and

each R^4 is independently alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro or thio.

29. The method of Claim 1 or 2, wherein the modulator is a compound of structural formula (II):



(II)

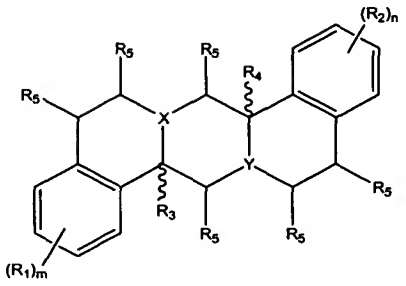
or a pharmaceutically available solvate or hydrate thereof, wherein:

X is O or S;

each R^1, R^2, R^3, R^4 and R^5 is independently hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro or thio; and

each R^6, R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro or thio.

30. The method of Claim 1 or 2, wherein the modulator is a compound of structural formula (III):



(III)

or a pharmaceutically available solvate or hydrate thereof, wherein:

n is 1, 2, 3, 4 or 5;

m is 1, 2, 3, 4, or 5;

each X and Y is independently C or N; and

each R^1, R^2, R^3, R^4 and R^5 is independently hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro or thio.

31. A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III).

32. A method for treating or preventing ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colorectal cancer, uterine cancer, stomach cancer, small intestine cancer, thyroid cancer, lung cancer,

kidney cancer, pancreas cancer, prostrate cancer, adult respiratory distress syndrome (ARDS), asthma, transcorneal freezing, cutaneous burns, ischemia or atherosclerosis in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III).

33. A method for treating or preventing vasoconstriction, autoimmune disorders or vascular occlusive disorders in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III).

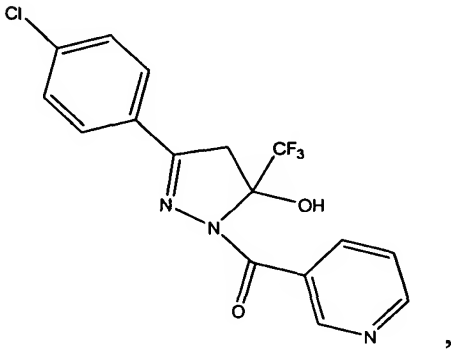
34. A method for treating or preventing vasoconstriction in cerebral arteries, systemic lupus erythematosus, rheumatoid arthritis, non-glomerular nephrosis, psoriasis, chronic active hepatitis, ulcerative colitis, Crohn's disease, Behçet's disease, chronic glomerulonephritis, chronic thrombocytopenic purpura, autoimmune hemolytic anemia, migraine headache, stroke, subarachnoid hemorrhage, or a vasospasm in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III).

35. A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, cardiovascular diseases, vasoconstriction, autoimmune disorders or vascular occlusive disorders in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III) and one or more agonists or antagonists of an Edg receptor.

36. A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, cardiovascular diseases, vasoconstriction, autoimmune disorders or vascular occlusive disorders in a subject comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III) and one or more drugs useful in treating or preventing cancers, acute lung diseases, acute inflammatory

exacerbation of chronic lung diseases, surface epithelial cell injury, cardiovascular diseases, vasoconstriction, autoimmune disorders or vascular occlusive disorders.

37. The method of Claim 28, wherein the modulator is a compound of a formula that is selected from the group consisting of:



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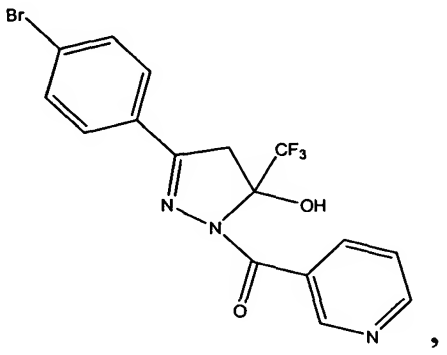

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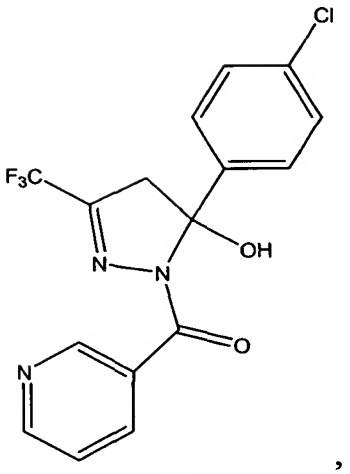

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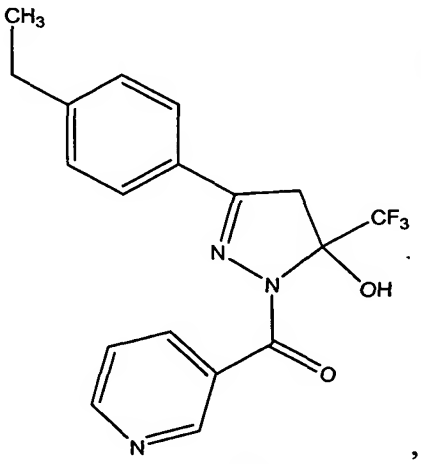

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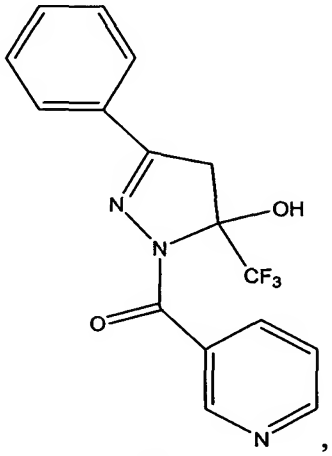

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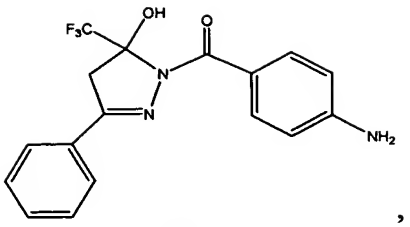

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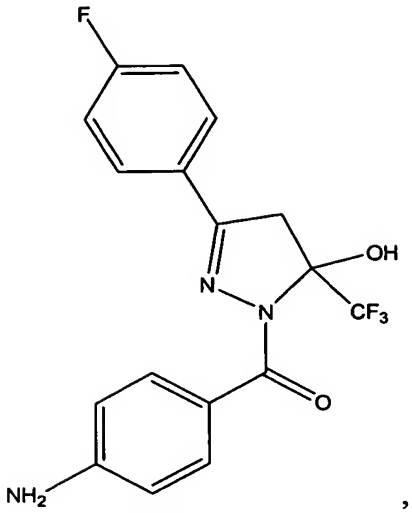

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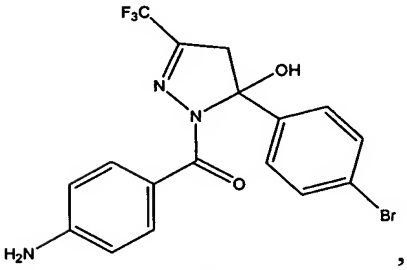

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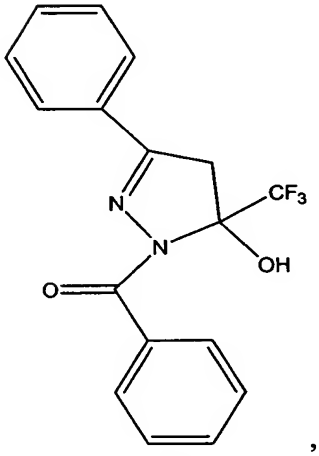

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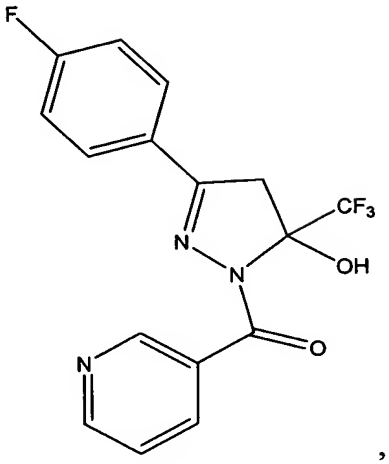

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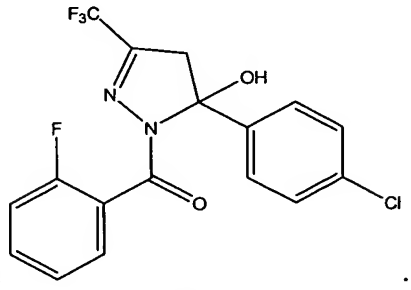
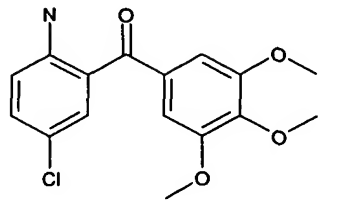


and 113.

38. The method of Claim 29, wherein the modulator is a compound of formula



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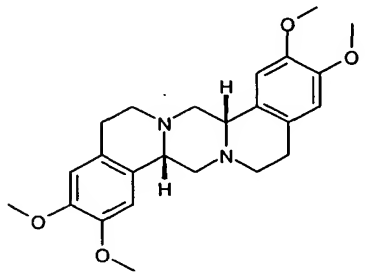
39. The method of Claim 30, wherein the modulator is a compound of formula



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40. The method of Claim 1 or 2, wherein the biological activity is an immune response.

41. The method of Claim 40, wherein the immune response is stimulated by S1P.

42. A method for treating or preventing a disorder in a subject, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III), wherein the compound of structural formula (I), (II) or (III) stimulates the immune system.

43. The method of Claim 42, wherein the subject suffers from an inherited immune deficiency.

44. The method of Claim 42, wherein the compound of structural formula (I), (II) or (III) is administered as an adjuvant to a vaccine.

45. The method of Claim 42, wherein the subject is infected with a virus.

46. The method of Claim 45, wherein the virus is selected from the group consisting of cytomegalovirus, herpes simplex virus I, herpes simplex virus II, influenza A virus, influenza B virus, hepatitis A virus, hepatitis B virus, hepatitis C virus, and human immunodeficiency virus.

47. A method for treating or preventing an immune disorder in a subject, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I), (II) or (III), wherein the immune disorder is characterized by inappropriate activation of the immune system.

48. The method of Claim 47, wherein the compound of structural formula (I), (II) or (III) suppresses the immune system of the subject.

49. The method of Claim 48, wherein the subject is afflicted with a disorder that is selected from the group consisting of systemic lupus erythematosus, rheumatic cardiatis, polymyosis, pemphigus, bullous dermatits herpetiformis, Stevens-Johnson syndrome, mycosis fungoides, dermatitis, ulcerative colitis, Crohn's disease, intractable sprue, idiopathic thrombocytopenic purpura, hemolytic anemia, erythroblastopenia, congenital hypoplastic anemia, osteoarthritis, rheumatoid arthritis, bursitis, acute gouty arthritis, epicondylitis, acute nonspecific tenosynovitis, multiple sclerosis, keratitis, irititis, irisocyclitis, chorioretinitis, choroiditis, optic neuritis, sarcoiodosis, Loeffler's syndrome, berylliosis, tuberculosis, sponylitis, tenosynovitis, psoriatic arthritis, and type I diabetes mellitus.

50. The method of Claim 48, wherein the subject is the recipient of a transplanted cell, tissue, or organ.